

**REMARKS**

The pending claims have been amended as indicated in the marked-up version above in response to the Examiner's comments. Applicants believe that the Examiner's concerns are addressed by these amendments and respectfully request reconsideration.

**Indefiniteness**

While applicants consider the terms "heteroalkyl", "heteroalkenyl", "heteroalkynyl" and "[hetero]forms thereof" to be clearly understood by those of skill in the art, and thus definite, those terms have been removed from the language of the amended claims in order to expedite prosecution. Each amended claim retains the list of specific substituents that was presented in the original claim and specification; thus the amended claims are fully supported by the original application and add no new matter.

Likewise, all uses of the term "noninterfering substituents" have been removed from the amended claims. While applicants find this term as explained in the specification to be clear to one of ordinary skill, to give adequate notice of the scope of the claimed invention, and to claim the invention as conceived and understood by the inventors, it has nevertheless been removed to expedite prosecution. Again, each amended claim retains the list of specific substituents that was presented in the original claim and specification; thus the amended claims are fully supported by the original application and add no new matter.

With these terms deleted from the claims, applicants believe the description "...wherein two of said optional substituents on adjacent positions can be joined to form a fused, an optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members..." is sufficiently clear and definite to allow one of ordinary skill to know what chemical structures fall within the scope of the claimed invention. The word "fused" was deleted as surplusage: where two groups on adjacent ring atoms are joined to form a new ring, that new ring is necessarily "fused".

As amended, the claims no longer recite or rely on any of the functional language to which the Examiner has objected: the claims recite clear and definite structural limitations to define the scope of the claimed invention. The Examiner's concern that one could not determine whether a given compound falls within the scope of the claims without making the compound and testing it has thus been addressed, and applicants believe the amended claims are definite and allowable.

The Examiner also mentions "issues about size and structure" and incorporates by reference the relevant comments from Papers No. 12 and 14; applicants are unsure whether this objection has been fully resolved by prior amendments. While most size-based claim limitations have been removed by previous amendment, claim 1 still defines one portion of the molecule by chain length where it states: "each of W and X is substituted or unsubstituted alkylene or alkenylene, each of 2-6Å." With respect to this size limitation, it is not clear to applicants why this would be considered indefinite. A specific chain length range is provided. The description in the specification clarifies how such lengths should be computed, when it describes  $L^1$  and  $L^2$ : the distance is measured with bond lengths placed end-to-end. As the Examiner has shown, specific bond lengths are readily found in the CRC Handbook of Chemistry and Physics, for example. One of ordinary skill would thus have no difficulty ascertaining which alkylene and alkenylene groups fall within the scope of the claims. It is unclear to applicants whether the Examiner objects to this limitation, and since it defines an easily understood, small and well-supported set of chemical structures, and clearly describes the invention as understood by the inventors, it has been retained in the current claims.

### Utility

The Examiner also questions whether the 'method of use' claims satisfy the utility requirement, since they recite alleviation of p38- $\alpha$  mediated conditions. Under the PTO Guidelines, the utility requirement is satisfied where *in vitro* enzyme activity is demonstrated as long as the target enzyme is associated with the disease state for which utility is asserted. The claimed compounds are inhibitors of p38, and especially p38- $\alpha$ . These enzymes are widely associated in the literature with specific disease states. Under *In re Brana*, the PTO has the burden to establish that

one of ordinary skill would reasonably doubt the utility asserted by the applicant. 51 F.3d 1560 (Fed.Cir. 1995). The Examiner has not here provided a *prima facie* case to show that one of ordinary skill would *more likely than not* doubt the asserted utility of these compounds; thus the applicants believe such objection is not appropriate.

Nevertheless, the limitations in the claims to p38- $\alpha$  mediated conditions has been eliminated by canceling claims 65-66 and re-writing claim 68 in independent form. The claims as amended recite treatment of a disease or condition selected from a list of specific disorders that is taken from the original specification and claims; hence no new matter has been added. Applicants believe this satisfies the requirement that at least one specific, credible, and substantial utility must be disclosed.

Furthermore, as stated in the disclosure, the compounds of the present invention are useful to treat p38 as well as p38- $\alpha$  mediated disorders (spec. at 2). P38 is strongly associated in the literature with numerous disorders, and the disorders for which p38 inhibitors are reported to be effective are included in the list of conditions for which the claimed invention is useful. Thus if the Examiner is challenging utility only based on the p38- $\alpha$  mediation connection, consideration must also be given to utility based on the broader p38 activity asserted. Such use is very strongly associated in the literature with the treatment of specified disorders: by 2002, at least three drug companies (not counting the applicant) had p38 inhibitors undergoing clinical trials. P. Cohen, Nature Reviews: Drug Discovery, April 2002, p. 309-15. Applicants believe the utility requirement is thus satisfied by assertion of p38 activity to prove utility, unless the Examiner provides evidence and arguments to show that one of ordinary skill would doubt that these particular compounds are useful for such treatments. Applicants believe that the Examiner has not presented sufficient basis to challenge the asserted utility of the 'method of use' claims, and in light of the present claim amendments, applicants believe no such objection is warranted. Removal of this objection is thus respectfully requested in light of the foregoing arguments.

Clerical Corrections

A typographical error in claim 1, which was repeated in claims 57 and 58, has been corrected by deletion of “alkyl-OOR” from the list of permitted groups for  $R^3$  and  $R^4$ .

Claim 12 has been made to depend from claim 1; it originally depended from claim 11 which has been canceled previously, and its dependency was not previously corrected.

Clarifying language was added to the description of  $R^3$  in claim 57; support for this description of  $R^3$  is found in the specification at page 13.

Claim 68 has been rewritten in independent form, incorporating language from canceled claim 66.

Claims 40 and 41 have been modified to make them consistent with the present version of claim 1. Support for the narrower descriptions of  $L^1$  and  $L^2$  is found in the originally presented claims and in the specification.

Claims 42-43 and 64-67 have been canceled.

## CONCLUSION

It is believed that the present claims overcome the Examiner's stated objections and are free of the art. Therefore, it is respectfully requested that claims 1, 3-7, 9, 12, 39-41, 45-46, 48-50, 52-56, 57-61, 63 and 68 be deemed allowable and pass to issue forthwith.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 219002029100.

Dated: September 15, 2004

Respectfully submitted,

By   
Michael G. Smith

Registration No.: 44,422  
MORRISON & FOERSTER LLP  
3811 Valley Centre Drive, Suite 500  
San Diego, California 92130  
(858) 720-5100